Journal of Cardiology (2009) **53**, 196—203

ELSEVIER

CARDIOLOGY
Official Journal of the Japanese College of Cardiology

www.elsevier.com/locate/jjcc

ORIGINAL ARTICLE

Levels of serum deoxyribonuclease I activity on admission in patients with acute myocardial infarction can be useful in predicting left ventricular enlargement due to remodeling

Jun Kuribara (MD)[a,*], Hiroshi Tada (MD)[b], Yasuyuki Kawai (MD)[c], Ren Kawaguchi (MD)[b], Hiroshi Hoshizaki (MD)[b], Kenichiro Arakawa (MD)[d], Michihiko Kitayama (MD)[c], Kouji Kajinami (MD, FJCC)[c], Masahiko Kurabayashi (MD, FJCC)[a], Shigeru Oshima (MD, FJCC)[b], Koichi Taniguchi (MD, FJCC)[b], Yoshihiko Kominato (MD)[e], Toshihiro Yasuda (PhD)[f]

[a] *Department of Cardiology, Gunma University Graduate School of Medicine, 39-15-3 Showa, Maebashi, Gunma 371-8511, Japan*
[b] *Division of Cardiology, Gunma Prefectural Cardiovascular Center, Maebashi, Japan*
[c] *Department of Cardiology, Kanazawa Medical University, Uchinada, Japan*
[d] *Third Department of Internal Medicine, Faculty of Medical Sciences, University of Fukui, Fukui, Japan*
[e] *Department of Legal Medicine, Gunma University Graduate School of Medicine, Maebashi, Japan*
[f] *Division of Medical Genetics and Biochemistry, Faculty of Medical Sciences, University of Fukui, Fukui, Japan*

Received 13 August 2008; received in revised form 23 October 2008; accepted 29 October 2008
Available online 4 January 2009

KEYWORDS
Acute myocardial infarction;
DNase I;
Left ventricular remodeling

Summary
Objectives: Serum deoxyribonuclease I (DNase I) activity has recently been highlighted as a potential diagnostic marker for the early detection of an acute myocardial infarction (AMI). We evaluated whether the serum DNase I activity was associated with the parameters of the left ventricular (LV) remodeling after an AMI.
Methods: We measured the serum DNase I activity in 45 patients with an AMI who were admitted to our hospital within approximately 4 h of the onset of their chest pain. We also evaluated the LV ejection fraction (LVEF), LV end-diastolic volume (LVEDV), and LV end-systolic volume (LVESV) of each patient by echocardiography at the time of admission and at 6 months after the onset of the AMI.

* Corresponding author. Tel.: +81 27 220 8153; fax: +81 27 220 8153.
E-mail address: kurihaj@yahoo.co.jp (J. Kuribara).

0914-5087/$ — see front matter
doi:10.1016/j.jjcc.2008.10.013

Results: The serum DNase I activity peaked at 3.5 ± 2.0 h after the onset of the symptoms in the patients with an AMI, thereafter exhibiting a time-dependent decline within 12 h, and a return to the basal level within 24 h in almost all cases. Neither the LVEF, LVEDV, nor LVESV in each patient on admission exhibited a significant correlation to the peak levels of the serum DNase I activity. Although there was no correlation between the peak DNase I activity and LVEF at 6 months after the onset, a significant positive correlation of the peak DNase I activity with LVEDV and LVESV ($r = 0.48$, $p < 0.001$ and $r = 0.34$, $p = 0.02$, respectively) was found.
Furthermore, the LVEDV at 6 months after the onset in the high DNase I activity group (>17.9 U/L) were significantly higher than those in the low DNase I activity group (≤17.9 U/L) (118.0 ± 28.2 ml vs 89.3 ± 25.4 ml, $p = 0.026$).
Conclusions: The serum DNase I activity level may predict LV enlargement associated with remodeling after an AMI.

Introduction

Left ventricular (LV) remodeling after an acute myocardial infarction (AMI) is the process of an infarct expansion followed by progressive dilation of the entire LV including the non-infarct myocardium, and is a major predictor of morbidity and mortality [1]. Although the precise molecular mechanisms of the LV remodeling are still unknown, apoptosis in the non-infarcted remote myocardium appears to be involved [2]. However, no association of any apoptosis-related biomarkers with LV remodeling has been elucidated.

Deoxyribonuclease I (DNase I, EC 3.1.21.1) is an endonuclease that preferentially attacks double-stranded DNA in a Ca^{2+}-dependent manner to produce oligonucleotides with 5′-phospho and 3′-hydroxy termini [3]. DNase I has been postulated to be one of the candidate nucleases that are responsible for internucleosomal DNA degradation during apoptosis [4,5]. In this context, it has been reported that the activity level of DNase I present in human myocardium is elevated in heart failure due to idiopathic dilated cardiomyopathy [6]. Our previous study demonstrated that the serum level of DNase I activity was abruptly elevated within approximately 3 h after the onset of symptoms, thereafter exhibiting a marked time-dependent decline within 12 h, and a return to the basal level within 24 h [7], and that because the peak serum level of the DNase I activity after the AMI onset was usually found within 4 h after the AMI onset at the latest, it might become a cardiac marker for diagnosing a superacute phase of an AMI [7]. However, no study has ever been performed to examine the relationship between the levels of the serum DNase I activity and LV function after AMI. Accordingly, in this study, we investigated whether the peak levels of serum DNase I activity after the onset of AMI could be associated with the parameters of LV remodeling, such as the LV ejection fraction (LVEF), LV end-diastolic volume (LVEDV), and LV end-systolic volume (LVESV), in the acute and chronic phases of an AMI, and also compared the results with those of creatine kinase (CK).

Methods

Study population

One hundred and fifty-eight consecutive Japanese patients with suspected AMI were admitted to our hospitals between August 2004 and August 2006. Considering the characteristics of the changes in the level of the serum DNase I activity after the AMI onset as described above [7], 93 patients with an AMI who were admitted to our hospital at more than 4 h after the symptom onset of the AMI were excluded from this study beforehand. Among the remaining 65 patients, 6 and 5 patients were excluded for inadequate echocardiographic image and old myocardial infarction, respectively, from the study. Furthermore, 9 patients declined to take part in this study, and ultimately 45 patients were enrolled. All of the study patients received emergent coronary angiography (CAG) and successful reperfusion therapy by primary coronary intervention (PCI) with stenting. The clinical diagnosis of an AMI was made according to the European Society of Cardiology/American College of Cardiology Committee criteria [8].

The study protocol conformed to the Declaration of Helsinki and was approved by the Human Ethics Committee of our institution; each subject included in the study gave written informed consent before study participation.

Echocardiography

All patients underwent two-dimensional echocardiography at the time of admission and 6 months after the onset of the AMI (Sonos 5500, Phillips Medical Systems, MA, USA). A standard imaging protocol was used based on the apical 4-chamber, 2-chamber, parasternal long- and short-axis views. These images were recorded and analyzed by two experienced blinded ultrasonographers. The LVEDV and LVESV were calculated by the modified Simpson's biplane method. The LVEF was calculated from the formula (LVEDV − LVESV) × 100%/LVEDV. These values were considered indicators of the magnitude of the LV remodeling.

Collection of blood samples and the measurement of the serum DNase I activity and CK levels

Blood samples were obtained from an antecubital vein at the time of admission, and every 3 h until the peak CK levels were determined. Furthermore, follow-up blood samples were obtained at 2, 3, 7, and 14 days, and 6 months after the onset of the AMI. The serum samples were prepared from each blood sample by centrifugation and stored at −80 °C until use.

Table 1 Clinical characteristics of the study patients.

	AMI patients
Total population	45
Age (years)	67 ± 11
Men	32 (71)
Coronary risk factor	
Cigarette smoking	20 (44)
Diabetes mellitus	16 (36)
Hypertension	28 (62)
Hypercholesterolemia	31 (52)
Obesity	10 (22)
Culprit lesions	
Left anterior descending	25 (56)
Left circumflex	9 (20)
Right coronary artery	11 (24)
STEMI	41 (91)
In-hospital medications	
ACEIs or ARBs	36 (80)
β-Blockers	14 (31)
Calcium antagonists	16 (36)
Diuretics	9 (20)

Data are presented as mean ± S.D. or number (%) of patients; STEMI, ST elevated myocardial infarction; ACEIs, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-II receptor antagonists.

The DNase I activity levels in the serum samples were measured by a single radial enzyme diffusion (SRED) method, as described previously [9,10]. One unit of the enzyme assayed corresponded to 0.6 ng of purified human DNase I [3]. The serum CK concentration was determined with an automated chemiluminescence system (Ciba Corning Diagnostics Corp., Medfield, MA, USA), in accordance with the manufacturer's instructions.

Statistical analysis

Continuous variables are expressed as the mean ± 1 standard deviation and the Student's *t*-test was used to compare the 2 groups. The Spearman's correlation coefficient was used to determine the relation between the peak DNase I, CK levels, and the echocardiographic parameters. Parameters were analyzed by parametric or non-parametric method with or without normality of distributions. A data analysis was performed with StatView software, version 5.0 (Abacus Concept, Inc., Berkley, CA, USA). A p-value <0.05 was considered statistically significant.

Results

Patient characteristics

The clinical characteristics of studied patients are shown in Table 1. There were 32 men and 13 women, and their mean age was 67 ± 11 years. The average time between the onset of symptoms and the hospital admission was 2.1 ± 1.2 h (range 0.2−3.9). Twenty-eight (62%) of the patients had hypertension, 31 (69%) hyperlipidemia, 16 (36%) diabetes mellitus, and 20 (44%) were current smokers. There were 4 patients with non-ST-elevation MI. None had any major adverse cardiac events, defined as a cardiac death, nonfatal AMI, or hospitalization due to heart failure, during a mean follow-up period of 7.0 ± 0.6 months.

All patients were administered aspirin and ticlopidine after the PCI. Thirty-six patients (80%) were treated with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-II receptor antagonists (ARBs), whereas 14 patients (31%) were treated with β-blockers, and 16 (36%) were treated with calcium antagonists. Diuretics were used in 9 patients (20%) with congestive heart failure (CHF).

Alterations in the serum DNase I activity levels following an AMI

The changes in the serum DNase I activity levels from the onset in patients with an AMI are shown

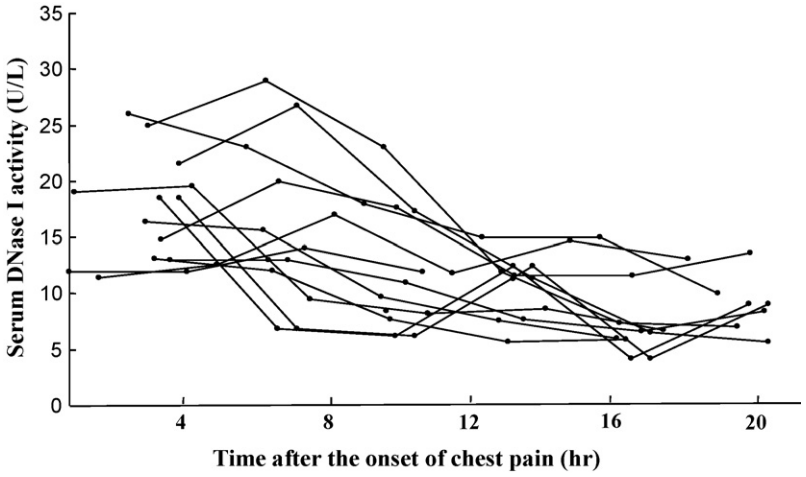

Figure 1 Changes in the serum DNase I activity level as a function of time from the onset in tens of patients with an AMI admitted to our hospital within 4 h.

in Fig. 1. The serum DNase I activity level peaked within 6 h after the onset of the symptoms in the patients with an AMI, thereafter showing a time-dependent decline within 12 h, and a return to the basal level within 24 h in almost all cases, confirming an alteration in serum DNase I activity levels of the patients after the onset reported previously [7].

The peak level of serum DNase I activity was 14.7 ± 5.6 U/L (range 6.9—25.7). The mean time from the onset of the symptoms to the peak level of the DNase I activity was 3.5 ± 2.0 h (range 0.2—6.0). The serum DNase I activity level exceeded the normal range, which was defined as a value >17.9 U/L [7] or the percent differences in the

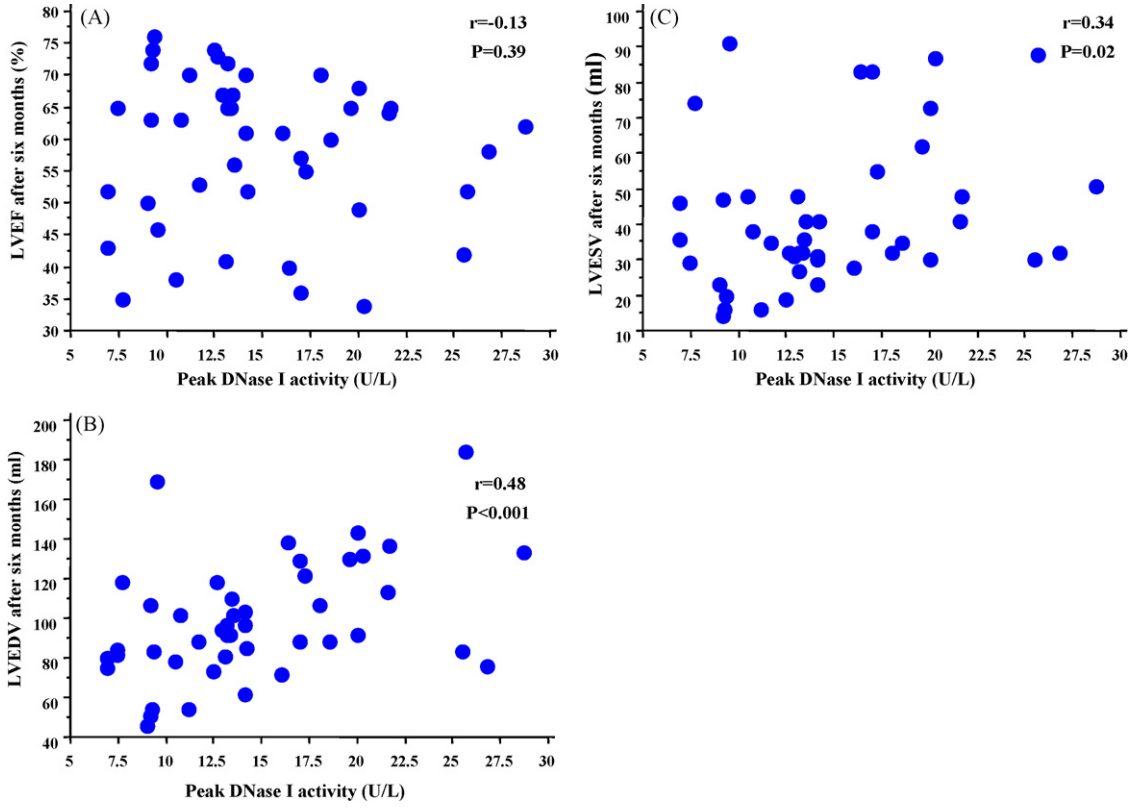

Figure 2 Correlation between the peak serum DNase I activity level and left ventricular ejection fraction (LVEF; A), end-diastolic volume (LVEDV; B), and end-systolic volume (LVESV; C) measured 6 months after the AMI.

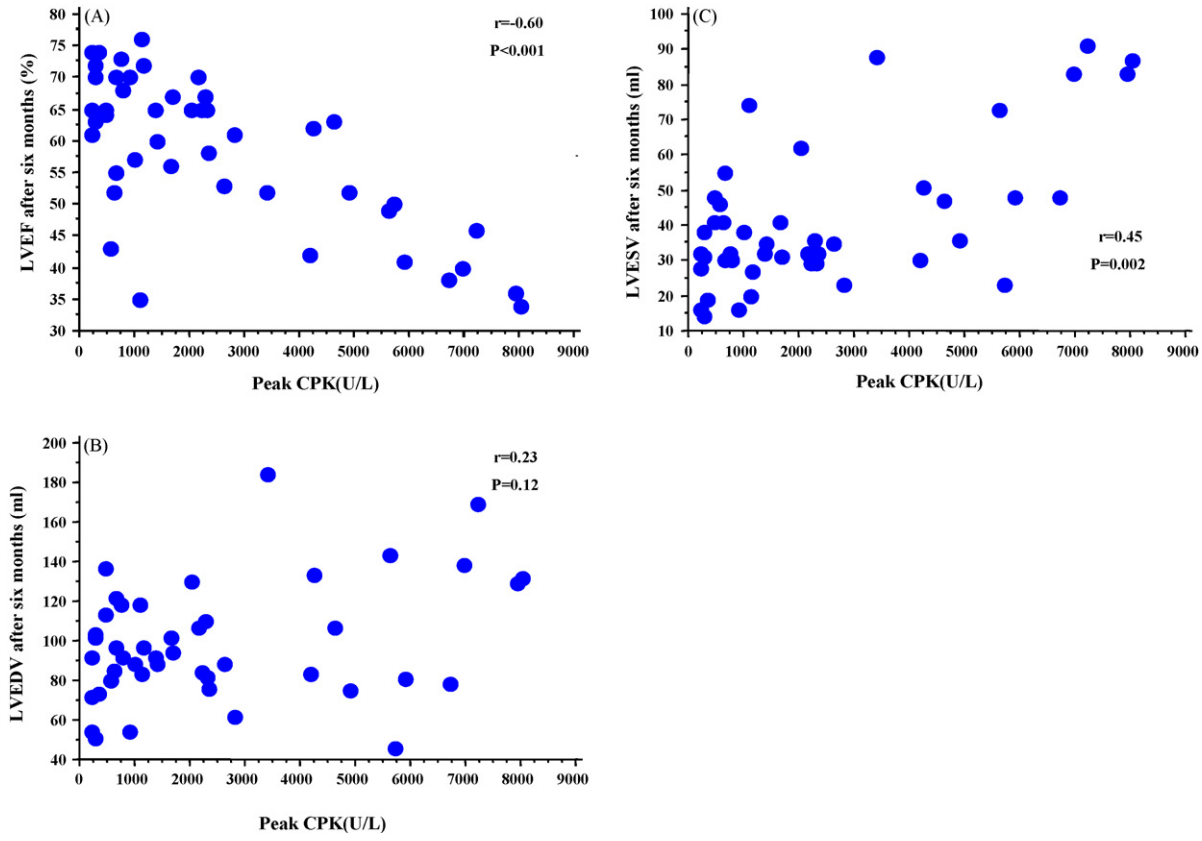

Figure 3 Correlation between the peak serum creatine kinase (CK) and and left ventricular ejection fraction (LVEF; A), end-diastolic volume (LVEDV; B), and end-systolic volume (LVESV; C) measured 6 months after the AMI.

serum DNase I activity at 3 h after the admission was >12.4% [11] in 33 (73%) patients. The peak level of the serum DNase I activity did not differ between the patients with and without hypertension ($p = 0.62$), hyperlipidemia ($p = 0.11$), diabetes mellitus ($p = 0.75$), or a current smoking habit ($p = 0.82$).

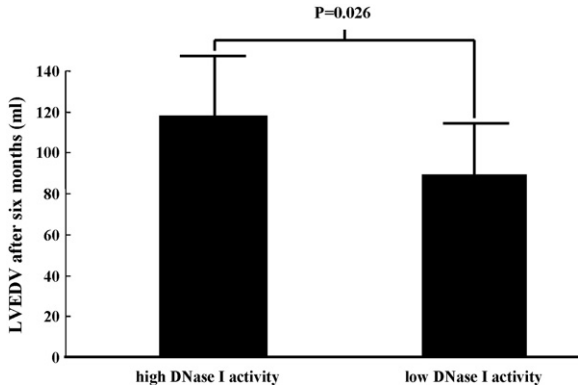

Figure 4 Comparison of the LVEDV 6 months after the AMI between the high DNase I group and the low DNase I group.

Relationship of the peak serum DNase I activity and CK levels with the echocardiographic parameters

The peak serum DNase I activity levels in patients was not correlated with LVEF, LVEDV, and LVESV on admission, and furthermore with the LVEF measured at 6 months after the AMI (Fig. 2A). However, significant correlations of the peak serum DNase I activity levels with the LVEDV ($r = 0.48$, $p < 0.001$) and LVESV ($r = 0.34$, $p = 0.02$) measured at 6 months after the AMI were found in a positive manner (Fig. 2B and C).

There was no significant difference found in the peak serum DNase I activity level and peak serum CK ($r = 0.11$, $p = 0.49$) levels.

The peak serum CK ($r = -0.60$, $p < 0.001$, Fig. 3A) levels were significantly correlated with the LVEF 6 months after the onset in a negative manner, whereas they were correlated with the LVESV 6 months after the AMI in a positive manner ($r = 0.45$, $p = 0.002$, Fig. 3C). However, there was no significant correlation between the peak CK level and LVEDV measured 6 months after the AMI ($r = 0.23$, $p = 0.12$, Fig. 3B).

Next, we divided these patients into a high DNase I activity group whose peak DNase I activity was above 17.9 U/L and a low DNase I activity group whose activity was less than 17.9 U/L according to the previous report [7]. The LVEDV at 6 months after the AMI in the high DNase I activity group was significantly higher than those in the low DNase I activity group (118.0 ± 28.2 ml vs 89.3 ± 25.4 ml, $p = 0.026$, Fig. 4). However, both LVESV and LVEF at 6 months after the AMI did not differ between the two groups.

Discussion

Major findings

In this clinical study, we confirmed that the peak levels of serum DNase I activity were observed at 3.5 ± 2.0 h after the onset of chest pain and exhibited a time-dependent decline, and returned to a normal level within about 24 h, which was consistent with our previous report [7]. Examination of the correlation between the peak serum DNase I activity levels on admission and echocardiographic parameters of the LV remodeling permitted us to demonstrate that the peak DNase I levels were significantly correlated with the LVEDV and LVESV 6 months after the onset of an AMI in a positive manner. However, there was no correlation between the peak DNase I activity level and the LVEF after 6 months. Furthermore, we found that the LVEDV at 6 months after the AMI was significantly higher in the high DNase I group than in the low DNase I group.

These findings may indicate that the peak levels of the serum DNase I activity can be a predictor of LV enlargement, but not of the LV function after an AMI; the higher the peak levels are, the larger the LV end-diastolic and end-systolic volumes are.

Serum DNase I activity levels in AMI patients

The treatment with the PCI procedures made the serum CK levels become elevated in the patients with an AMI, whereas the serum DNase I did not. These findings allowed us to clarify that the serum DNase I activity level did not become affected by the PCI procedure in a different manner than that for the CK in the AMI-patients. According to a number of previous reports, DNase I is secreted by exocrine glands, such as the pancreas and parotid gland, into the alimentary tract [12—14]. Furthermore, DNase I has also been detected in various tissues, including the small intestine, stomach, kidney, heart, liver, and pituitary gland, in which the DNase I is stored in the secretory granules of the cells and secreted into the lumen [15,16]. It is plausible to suggest that DNase I may be secreted from granules in the myocardium as well as brain natriuretic peptide, when triggered by myocardial ischemia, and may take time until it can be stored in the granules after its secretion. Therefore, the DNase I might not exhibit an elevated serum level after the PCI procedure in patients with an AMI. In this study, 12 patients did not exhibit any distinct alterations in the serum DNase I activity levels irrespective of whether or not it was early after the onset of the AMI. Recently, we demonstrated that the serum DNase I activity level could be a marker of transient myocardial ischemia after PCI and vasospastic angina pectoris [10,17]. Accordingly, it is plausible that the DNase I did not become elevated in those patients because of the transient myocardial ischemia induced by the prodromal angina before the onset of the AMI. Further study will be needed to elucidate the effect of the prodromal angina on the DNase I levels in patients with an AMI.

Peak serum DNase I activity level as a marker for LV enlargement

The progressive LV enlargement was associated with an increased incidence of morbidity and mortality after the AMI [1]. Although the precise molecular mechanisms of the LV remodeling are still unknown, myocyte apoptosis in the non-infarcted remote myocardium appears to be involved [2]. DNase I has been postulated to be one of the candidate nucleases that are responsible for the internucleosomal DNA degradation during apoptosis [4,5]. Recently, we reported that the serum DNase I activity level became elevated transiently and abruptly after the onset of an AMI [7]. Oliveri et al. [18,19] reported that DNase I is internalized by human cells upon binding with mannose 6-phosphate receptors and behaves as a transcriptional factor which modulates the Fas expression leading to the induction of apoptosis. Most of the cell death in the first 2—4 h following a coronary occlusion has been known to occur by apoptosis from rat myocardial infarction models [20—22]. On the basis of these findings, we postulated that the serum DNase I may induce myocardial apoptosis followed by LV remodeling. This clinical study demonstrated that the peak DNase I activity level was positively associated with the LVEDV and LVESV, but not with the LVEF, 6 months after the onset of the AMI, whereas the peak CK levels were significantly associated with the LVEF after 6 months in a negative manner. On the other hand, the peak

DNase I activity level did not correlate with the CK levels which are used in assessing the cellular necrosis and reflect the infarct size after an AMI. Therefore, these findings that the DNase I did not reflect the infarct size, but were associated with the LV dilation during the chronic phase permitted us to speculate that the peak DNase I activity levels in the acute phase of an AMI may predict the LV enlargement unlike the CK level.

Limitations

First, our sample size was small. However, the results of this study will facilitate further studies using larger numbers of patients to evaluate whether the serum DNase I activity level is a predictive marker for LV remodeling. Secondly, it remains to be clarified how myocardial ischemia induced by an AMI could elevate the levels of the serum DNase I activity in the patients. It has been demonstrated that both the level of the DNase I activity and DNase I gene expression in cultured human cells increases under hypoxia in comparison with normoxia, suggesting that hypoxia allows the serum DNase I activity to rise, perhaps due to up-regulation of the DNase I gene [23,24]. Hypoxia-induced up-regulation of the gene expression can partly account for how the levels of the DNase I activity in the serum of the patients are elevated in response to ischemia. However, further clarification of the mechanism responsible for the DNase I elevation and physiological significance of the DNase I in myocardial ischemia will undoubtedly have important biological and clinical implications. Finally, the LV remodeling after an AMI is affected by the early reperfusion and drug treatment [25—28]. All the patients in this study underwent a successful PCI within 6 h after the onset of the AMI and 36 patients (80%) were treated with ACEIs or ARBs which prevent LV remodeling. Therefore, we consider that these factors did not affect the association between the peak DNase I activity and LVEDV and LVESV.

Conclusions

The serum DNase I activity level may predict the LV enlargement and may be a potential tool for risk stratification after an AMI.

Acknowledgments

This study was supported in part by Grants-in-Aid from the Japan Society for the Promotion of Science (19390184 to T.Y.) and by a grant from the Gunma Prefecture Government, Japan. We are indebted to Mr. Yasuyuki Kobayashi and Ms. Mari Kurata, cardiac fellows, and the staff in the cardiac echo section at the Gunma Prefectural Cardiovascular Center for their important contribution to this study.

References

[1] Pfeffer MA, Braunwald E. Ventricular remodeling after myocardial infraction. Experimental observations and clinical implications. Circulation 1990;81:1161—72.
[2] Abbate A, Biondi-Zoccai GGL, Bussani R, Dobrina A, Camilot D, Feroce F, Rossiello R, Baldi F, Silvestri F, Biasucci LM, Baldi A. Increased myocardial apoptosis in patients with unfavorable left ventricular remodeling and early symptomatic post-infarction heart failure. J Am Coll Cardiol 2003;41:753—60.
[3] Yasuda T, Awazu S, Sato W, Iida R, Tanaka Y, Kishi K. Human genetically polymorphic deoxyribonuclease: purification, characterization and multiplicity of urine deoxyribonuclease I. J Biochem 1990;108:393—8.
[4] Rauch F, Polzar B, Stephan H, Zanotti S, Paddenberg R, Mannherz HG. Androgen ablation leads to an upregulation and intranuclear accumulation of deoxyribonuclease I in rat prostate epithelial cells paralleling their apoptosis elimination. J Cell Biol 1997;137:909—23.
[5] Mannherz HG, Peitsch MC, Zanotti S, Paddenberg R, Polzar B. A new function for an old enzyme: the role of DNase I in apoptosis. Curr Top Microbiol Immunol 1995;198:161—74.
[6] Yao M, Keogh A, Spratt P, dos Remedios CG, Kiessling PC. Elevated DNase I levels in human idiopathic dilated cardiomyopathy: the role of DNase I in apoptosis? J Mol Cell Cardiol 1996;28:95—101.
[7] Kawai Y, Yoshida M, Arakawa K, Kumamoto T, Morikawa N, Masamura K, Tada H, Ito S, Hoshizaki H, Oshima S, Taniguchi K, Terasawa H, Miyamori I, Kishi K, Yasuda T. The diagnostic use of serum deoxyribonuclease I activity as a novel early-phase marker in acute myocardial infarction. Circulation 2004;109:2398—400.
[8] Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined: a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959—69.
[9] Nadano D, Yasuda T, Kishi K. Measurement of deoxyribonuclease I activity in human tissues and body fluids by a single radial enzyme-diffusion method. Clin Chem 1993;39:448—52.
[10] Takeshita H, Nakajima T, Mogi K, Kaneko Y, Yasuda T, Iida R, Kishi K. Rapid quantification of DNase I activity in one-microliter serum samples. Clin Chem 2004;50:446—8.
[11] Arakawa K, Kawai Y, Kumamoto T, Morikawa N, Yoshida M, Tada H, Kawaguchi R, Taniguchi K, Miyamori I, Kominato Y, Kishi K, Yasuda T. Serum deoxyribonuclease I activity can be used as a sensitive marker for detection of transient myocardial ischemia induced by percutaneous coronary intervention. Eur Heart J 2005;26:2375—80.
[12] Laskowski M. Deoxyribonuclease I. In: Boyer PD, editor. The enzymes, vol. 4, 3rd ed. New York: Academic Press; 1971. p. 281—311.
[13] Rohr G, Mannherz HG. Isolation and characterization of secretory actin: DNase I complex from rat pancreatic juice. Eur J Biochem 1978;89:151—7.

[14] Lacks SA. Deoxyribonuclease I in mammalian tissues. Specificity of inhibition by actin. J Biol Chem 1981;256: 2644—8.
[15] Shimada O, Ishikawa H, Tosaka-Shimada H, Yasuda T, Kishi K, Suzuki S. Detection of deoxyribonuclease I along the secretory pathway in Paneth cells of human small intestine. J Histochem Cytochem 1998;46:833—40.
[16] Tsutsumi S, Kaneko T, Asao T, Kuwano H, Kudo S, Takeshita H, Yasuda T, Kishi K. DNase I is present in the chief cells of human and rat stomachs. Histochem J 2001;33: 531—5.
[17] Morikawa N, Kawai Y, Arakawa K, Kumamoto T, Miyamori I, Akao H, Kitayama M, Kajinami K, Lee JD, Takeshita H, Kominato Y, Yasuda T. Serum deoxyribonuclease I activity can be used as a novel marker of transient myocardial ischemia: results in vasospastic angina pectoris induced by provocation test. Eur Heart J 2007;28:2992—7.
[18] Oliveri M, Daga A, Cantoni C, Lunardi C, Millo R, Puccetti A. DNase I mediates internucleosomal DNA degradation in human cells undergoing drug-induced apoptosis. Eur J Immunol 2001;31:743—51.
[19] Oliveri M, Daga A, Lunardi C, Navone R, Millo R, Puccetti A. DNase I behaves as a transcription factor which modulates Fas expression in human cells. Eur J Immunol 2004;34:273—9.
[20] Cheng W, Kajstura J, Nitahara JA, Li B, Reiss K, Liu Y, Clark WA, Krajewski S, Reed JC, Olivetti G, Anversa P. Programmed myocyte cell death affects the viable myocardium after infarction in rats. Exp Cell Res 1996;226:316—27.
[21] Fliss H, Gattinger D. Apoptosis in ischemic and reperfused rat myocardium. Circ Res 1996;79:949—56.
[22] Bialik S, Geenen DL, Sasson IE, Cheng R, Horner JW, Evans SM, Lord EM, Koch CJ, Kitsis RN. Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53. J Clin Invest 1997;100:1363—72.
[23] Kominato Y, Ueki M, Iida R, Kawai Y, Nakajima T, Makita C, Itoi M, Tajima Y, Kishi K, Yasuda T. Characterization of human deoxyribonuclease I gene (DNAse 1) promoters reveals the utilization of two transcription-starting exons and the involvement of Sp1 in its transcriptional regulation. FEBS J 2006;273:3094—105.
[24] Kominato Y, Iida R, Nakajima T, Tajima Y, Takagi R, Makita C, Kishi K, Ueki M, Kawai Y, Yasuda T. Hypoxia induced upregulation of the deoxyribonuclease I gene in the human pancreatic cancer cell line QGP-1. Biochim Biophys Acta 2007;1770:1567—75.
[25] Bolognese L, Neskovic AN, Parodi G, Cerisano G, Buonamici P, Santoro GM, Antoniucci D. Left ventricular remodeling after primary coronary angioplasty: patterns of left ventricular dilation and long-term prognostic implications. Circulation 2002;106:2351—7.
[26] Waldecker B, Waas W, Habersbosh W, Voss R, Heizmann H, Tillmanns H. Long-term follow-up after direct percutaneous transluminal coronary angioplasty for acute myocardial infarction. J Am Coll Cardiol 1998;32:1320—5.
[27] St John Sutton M, Pfeffer MA, Plappert T, Rouleau JL, Moye LA, Dagenais GR, Lamas GA, Klein M, Sussex B, Goldman S, Menapace FJ, Parker JO, Lewis S, Setier F, Gordon DF, et al. Quantitative two-dimensional echocardiographic measurements are major predictors of adverse cardiovascular events after acute myocardial infarction: the protective effects of captopril. Circulation 1994;89:68—75.
[28] Nishikimi T, Yamagishi H, Takeuchi K, Takeda T. An angiotensin II receptor antagonist attenuates left ventricular dilation after myocardial infarction in the hypertensive rat. Cardiovasc Res 1995;29:856—61.